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Horizon Scanning Technology Prioritising Summary Update

T-Stat for the detection of ischaemia

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Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

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This Horizon scanning prioritising summary was prepared by Ben Ellery, Linda Mundy and Professor Janet Hiller from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, School of Population Health and Clinical Practice, Mail Drop DX 650 545, University of Adelaide, Adelaide, SA, 5005.

PRIORITISING SUMMARY: UPDATE 2010

REGISTER ID: **000418 (REFERRAL)**

NAME OF TECHNOLOGY: **T-STAT ISCHAEMIA DETECTION SYSTEM**

PURPOSE AND TARGET GROUP: **FOR THE ASSESSMENT OF OXYGEN IN TISSUES IN POTENTIALLY ISCHAEMIC IN PATIENTS**

2010 SAFETY AND EFFECTIVENESS ISSUES:

Researchers in the Netherlands investigated the use of T-Stat among patients who underwent gastrointestinal anastomoses.[1] The study (n=44) aimed to determine feasibility of T-stat during gastrointestinal surgery and stability in determining levels of micro-vascular oxygen saturation.[2] Consecutive colorectal (n=30) and oesophageal (n=14) resections were performed with uncomplicated anastomoses and levels of haemoglobin oxygen saturation (StO_2) were measured at critical points in the procedures. Measurements of StO_2 were conducted using a sterile hand-held probe on serosal or adventitial tissue, each taking about five to ten seconds to complete. In oesophageal resections, mean StO_2 was stable before and after anastomosis in the proximal oesophagus (before: 66 ± 4.6, after: 68.3 ± 6%) and the gastric conduit （before: 70.6 ± 8.6, after: 69.8 ± 8.0%) (Figure 1).

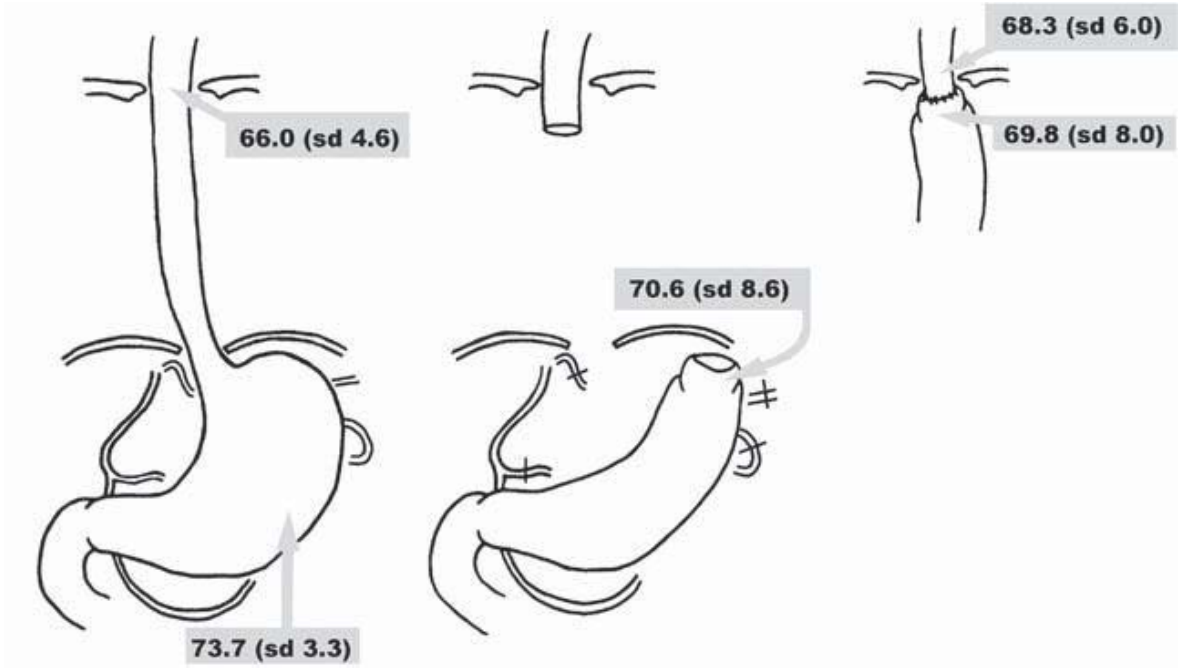

Figure 1 StO_2 (% oxyhaemoglobin) during oesophageal resection. Mean values (sd = standard deviation) for oesophagus proximal to the resection line after thoracotomy, proximal part of the gastric conduit in abdominal position and completed anastomosis (Karliczek et al 2008).

[1] Anastomosis is the surgical joining of primarily tubular parts.
[2] Publication during 2008 justified inclusion of this research in Prioritising Summary 2009, but due to omission at that time, the work is now presented in this update for 2010.

Mean colorectal StO_2 before and after anastomosis increased in the proximal part (71.3 ± 8.4 to 76.6 ± 8.2%; $p<0.005$). Mean StO_2 in the distal part remained stable (72.4 ± 6.6 to 74.8 ± 6.7%) (Figure 2).

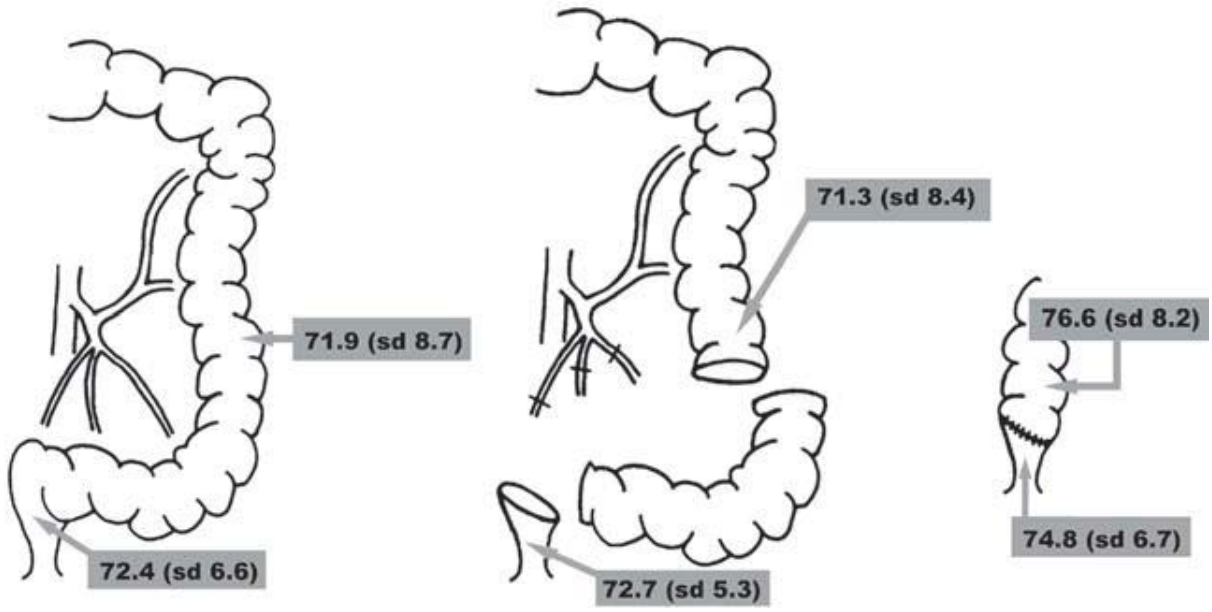

Figure 2 StO2 (% oxyhaemoglobin) during colorectal resection. Mean values (standard deviation) for distal colon/rectum, proximal colon during resection and completed anastomosis (Karliczek et al 2008).

Monitoring of systemic oxygen as part of standard operating procedure was reported, presumably to validate that T-Stat measures were a reflection of local tissue oxygenation, although the authors do no specifically state this. Within the limitations of this study, these results indicate that T-Stat can be easily used for intraoperative measurement of localised tissue oxygen saturation, with small variation at both surgical sites examined. One shortfall of this study is that no direct assessment of a comparator was undertaken. Alternative technologies for measurement of tissue oxygenation were reported, but these are limited in their acceptance due to various liabilities (Table 1).

In routine practice, surgeons subjectively assess intra-operative intestinal microcirculation based on colour and pulsating blood flow at the margins of dissected segments. This is considered the gold standard, yet no clear comparisons of sensitivity and specificity for T-stat with this standard have been made. Such data may be useful for informing possible comparative studies in the future. A conflict of interest issue is noted for one author of this study who is CEO of the company which manufactures the T-Stat, Spectros Corporation (Karliczek et al 2008) (level IV diagnostic evidence).

Table 1 Characteristics of technologies for intraoperative evaluation of tissue oxygenation (adapted from Karliczek et al 2008).

Technique	Assets	Liabilities
Laser Doppler flowmetry	Easy to perform during operation	Repeated measurements necessary; time consuming Tissue contact required; can disturb local blood flow Pulsatile blood flow required
Scanning laser Doppler flowmetry	Evaluation of larger surfaces	Requires (pulsatile) flow Relatively complicated Relatively long duration of measurement (~2 min)
Near-infrared spectrometry	Evaluation of deep tissue samples Low standard deviation of measurements No pulsatile blood flow required	Large tissue samples due penetration depth of light
Visible light spectroscopy (T-Stat)	Evaluation of small tissue samples No tissue contact needed No pulsatile blood flow required	Point measurements
Fluorescence videography	No tissue contact needed Evaluation of larger surfaces	Requires injection of fluorescent dyes Position-dependent measurements
Intramucosal pH	High accuracy in prediction of anastomic leakage	Necessity to leave catheters No real-time measurements

An American study used T-Stat to assess oxygen saturation (StO_2) differences between donor and recipient twins before and after laser ablation therapy for twin-twin transfusion syndrome (TTTS). TTTS is a complication of pregnancy, and in this context 'donor' and 'recipient' do not have the same definitions as conventionally used in therapeutic transfusion or transplant procedures. In TTTS, abnormal blood flow occurs from one twin (the 'donor') to the other twin (the 'recipient') via blood vessels in the common placenta. Identical monochorionic twins have vessels that connect on the surface of the placenta, and normally, blood flows from one twin to the other with a balance in both directions. TTTS results when this imbalance is disrupted and disproportionate flow of blood occurs between the twins (Mater Health Services 2010). Ten women with TTTS underwent the laser procedure which uses photocoagulation of communicating blood vessels to disrupt the TTTS process.[3] Percentage of StO_2 was measured using T-Stat with an endoscopic probe through the operating channel. As a means of standardising measurements, the probe was placed over the skin covering the hepatic area of donor and recipient twins. Levels of StO_2 were also measured at the placental surfaces in the territory of each twin. Skin measures of StO_2 for donor and recipient twins were obtainable for nine women prior to and after laser ablation. Mean StO_2 measures in donor and recipient skin before ablation were 21.6 ± 6.2 and 31.2 ± 8.6 per cent, respectively (p=0.01). After ablation, donor and recipient skin measures were 25.6 ± 6.5 and 27 ± 5.2 per cent, respectively (NS). The 18.5 per cent StO_2 increase in donor skin was significant (p=0.03), however

[3] This is another study published during 2008 but omitted from Prioritising Summary 2009. Consequently it is documented in this update.

the 13.5 per cent decrease in recipient skin was not, indicating an increased flow of oxygenated arterial blood to the donor. Reliable measurements for placenta were possible in five women. Before ablation, StO_2 measures of donor and recipient placenta were 25.6 ± 8.7 and 24 ± 4.1 per cent, respectively (NS). Post-ablation, donor and recipient placenta measures were 27.8 ± 7 and 36.8 ± 9.6 per cent, respectively (p=0.12). The 8.6 per cent StO_2 increase in donor placenta was not significant (p=0.47), whereas the 53.3 per cent increase in recipient placenta was significant (p=0.04), indicating that the 'dumping' of relatively deoxygenated blood from the donor to the recipient had been alleviated by the laser procedure. Results from the skin and placenta, taken together, show that laser ablation successfully corrected the non-admixing of deoxygenated and oxygenated blood. This supports the feasibility of T-Stat for measurement of StO_2 during in utero laser ablation to treat TTTS. However, the small sample size of the study is cause for careful interpretation. Further studies may help determine broader in utero applications for T-Stat (Quintero et al 2008) (level IV diagnostic evidence).

A case report documented the use of T-Stat during surgery for large bilateral IIA[4] aneurysms in a 66-year-old male. One serious complication of IIA aneurysm repair is colon ischaemia. Accordingly, the patient's oxygen levels were measured during and after the endovascular surgery. No changes in colon oximetry were detected (Lee & Dawson 2009) (level IV diagnostic evidence).

OTHER ISSUES:

Research pertaining specifically to T-Stat for the measurement of tissue oxygen saturation was sparse during 2009. Work on other technologies used in tissue oximetry was more prominent. One such technology, near-infrared spectroscopy (NIRS), has received positive attention since the 2009 Prioritising Summary, which focused on the limitations of NIRS. Some research has supported NIRS as a valuable alternative for the assessment of StO_2 levels in scenarios where visible light spectroscopy devices such as T-Stat are inappropriate (Beilman & Blondet 2009; Kussman et al 2009). For example, in procedures involving measurements through thick skin or transcranially, or larger tissue volumes, T-Stat would have limited use. However, NIRS could provide reliable data in these situations (Benaron et al 2004; Karliczek et al 2008).

The most recent data relating to T-Stat comes from a 2010 pilot study which investigated ischaemia in swine (n=8). Adult pigs underwent laparotomy to transect gastric tissue in vivo. Local gastric StO_2 measurements were taken in proximity to gastric staple lines, with significant ($p<0.05$) decreases in mucosal and serosal tissues compared with baseline levels. This was in spite of an absence of visible signs of ischaemia, such as colour changes or decreased pulsation. These results support the

[4] Internal iliac artery.

thought that transient or small degrees of ischaemia, which can contribute to the development of surgical complications, are not readily identified by subjective measures. This small-scale animal study demonstrates that T-Stat could assist surgeons identify ischaemic patients missed by non-quantitative assessment (Myers et al 2010) (level IV diagnostic evidence).

2010 SUMMARY OF FINDINGS:

None of the sources examined made a direct comparison of T-Stat with other valid technologies or techniques. The studies offer only low level evidence for the effectiveness of this technology. However, T-stat was demonstrated to be easily used for precise measurements of tissue oxygenation in a variety of settings. In particular, it may offer a diagnostic advantage over the subjective judgement routinely used to assess localised tissue oxygen levels intra-operatively, thereby reducing the risk of unmanaged ischaemia during surgical procedures. Larger studies with more attention to clinical outcomes are still required.

2010 HEALTHPACT ACTION:

There is a clear need for effective monitoring of tissue oxygen saturation in potentially ischaemic patients across a variety of clinical settings. T-Stat is a technology which shows promise for a number of clinical applications over conventional subjective methods of discerning signs of ischaemia, but comparative studies with alternative devices used in tissue oximetry are lacking. Larger studies with higher levels of evidence are necessary to further validate the clinical value of T-Stat. HealthPACT have therefore recommended that this technology be monitored for further information in 24-months.

2010 NUMBER OF INCLUDED STUDIES:

Total number of studies	3
Level IV diagnostic evidence	3

2010 REFERENCES:

Beilman, G. J. & Blondet, J. J. (2009). 'Near-infrared spectroscopy-derived tissue oxygen saturation in battlefield injuries: a case series report', *World J Emerg Surg*, 4, 25.

Benaron, D. A., Parachikov, I. H. et al (2004). 'Continuous, noninvasive, and localized microvascular tissue oximetry using visible light spectroscopy', *Anesthesiology*, 100 (6), 1469-1475.

Karliczek, A., Benaron, D. A. et al (2008). 'Intraoperative assessment of microperfusion with visible light spectroscopy in esophageal and colorectal anastomoses', *Eur Surg Res*, 41 (3), 303-311.

Kussman, B. D., Wypij, D. et al (2009). 'Cerebral oximetry during infant cardiac surgery: evaluation and relationship to early postoperative outcome', *Anesth Analg*, 108 (4), 1122-1131.

Lee, E. S. & Dawson, D. L. (2009). 'The Management of Large Bilateral Internal Iliac Artery Aneurysms Using the T-Stat Colon Oximeter', *Ann Vasc Surg*.

Mater Health Services (2010). *Twin to Twin Transfusion Syndrome* [Internet]. Available from: http://www.mater.org.au/Home/Services/Maternal-Fetal-Medicine/Twin-to-Twin-Transfusion-Syndrome.aspx [Accessed 9th February].

Myers, C. J., Mutafyan, G. et al (2010). 'Mucosal and serosal changes after gastric stapling determined by a new "real-time" surface tissue oxygenation probe: a pilot study', *Surg Obes Relat Dis*, 6 (1), 50-53.

Quintero, R. A., Chmait, R. H. et al (2008). 'In utero fetal oximetry via visible light spectroscopy in twin-twin transfusion syndrome', *Am J Obstet Gynecol*, 199 (6), 639 e631-634.

PRIORITISING SUMMARY (2009)

REGISTER ID: **000418 (REFERRAL)**

NAME OF TECHNOLOGY: **T-STAT ISCHAEMIA DETECTION SYSTEM**

PURPOSE AND TARGET GROUP: **FOR THE ASSESSMENT OF OXYGEN IN TISSUES IN POTENTIALLY ISCHAEMIC IN PATIENTS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☒	No	
☐	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
USA		✓	
UK	✓		

IMPACT SUMMARY:

Spectros Corporation manufactures the T-Stat® ischaemia detection system for the assessment of oxygen levels in tissues. The device would be used during various procedures which require accurate measurement of tissue oxygen levels, such as vascular or gastro-intestinal surgery. The T-Stat would be mainly used in hospital or other surgical clinics.

2009 BACKGROUND

Ischaemia is the inadequate supply of blood to a tissue, resulting in damage to the tissue due to a lack of oxygen and the subsequent built up of metabolic waste. Reduced blood flow can occur due to several factors such as compromised cardiac function, blood vessel constriction or blockage, or changes to local blood flow. Ischaemia is an important clinical consequence of many surgical and medical procedures and a variety of medical conditions including atherosclerosis which may lead to mesenteric ischemia.

The T-Stat system uses reflectance spectroscopy to measure the level of oxygen saturated haemoglobin in tissues (Figure 1). Oxygenated and deoxygenated haemoglobin have different absorption spectra under visible light, which can be used to calculate their relative concentrations. Visible light is used to illuminate a tissue through an optical fibre. Detection optical fibres gather the reflected light and pass it to a spectrophotometer where absorption is measured and the level of oxygen saturated haemoglobin in the tissue can be calculated. The T-Stat has several probes available for different applications including buccal or gastro-intestinal monitoring.

Figure 3 The T-Stat monitor with buccal probe and endoscopic catheter

Using the T-Stat monitor during various medical and diagnostic procedures would allow medical staff to assess the risk of ischaemia. If ischaemia is detected the medical specialist can take steps to alleviate the problem including the restoration of blood flow by removing clamps or by locating blood vessel blockages. This would prevent the serious consequences and associated morbidity caused by ischaemia.

2009 Clinical Need and Burden of Disease

Ischaemia due to many factors: acute or chronic disease, or surgical or medical procedures. As a result of this diversity of causes, data on the incidence and prevalence in Australia and New Zealand are lacking. Although ischaemia is a complication in many individual diseases or medical procedures, this data is not collated to give a global burden of ischaemia. To illustrate part of the burden of ischaemia an example is given for which some data exist. Intestinal ischaemia can occur subsequent to abdominal aorta surgery. There were 6,343 hospital separations in

2006-07 for abdominal aortic aneurysm in Australia. In a study investigating intestinal ischaemia after abdominal aorta surgery, it was found that up to 30 per cent of patients had ischaemia as detected by colonoscopic biopsy (Welch et al 1998). This is likely to be just a small part of the burden caused by ischaemia. Other areas where ischaemia detection may be important are cardiac surgery, gastrointestinal surgery, neonatal surgery.

2009 DIFFUSION

No evidence was found of T-Stat usage in Australia.

2009 COMPARATORS

Near infrared spectroscopy (NIRS) is used currently to assess the level of oxygen in tissues, however, this method lacks high quality diagnostic capabilities as normal ranges in tissues can be very broad. NIRS relies on an adequate blood flow, and may therefore fail under conditions of hypo-perfusion, which may be of importance as ischaemia may result from hypo-perfusion (Benaron et al 2004).

2009 SAFETY AND EFFECTIVENESS ISSUES

Several studies have utilised the T-Stat system to monitor tissue oxygenation in a variety of procedures. In addition, the system has been widely evaluated in animal studies which are not included in this prioritising summary.

A preliminary study investigated the T-Stat in pigs and human subjects. The pig model was used for validation of the device. The human arm of the study investigated normoxia, hypoxia, and local ischaemia. Results are reported in Table 1 (Benaron et al 2004) (level IV diagnostic evidence).

Table 2 T-Stat determination of oxygen levels in various induced states

T-Stat measurement	Oxygen levels[5]
Normoxia	
Enteric mucosal (n=50)	69 ± 4 %
Skin (n=20)	72 ± 16 %
Buccal mucosal (n=21)	77 ± 3 %
Hypoxia	
Eosophageal mucosal (n=3)	56 ± 6
Local ischaemia	
Partial Finger occlusion (n=5)	34*

* SD not reported

The evaluation of the T-Stat for colon ischaemia diagnosis was documented in a case report of an endovascular aneurysm repair (EVAR). The T-Stat probe was introduced during a colonoscopy and basal colon mucosal oxygen saturation (CMOS) was determined to be 57 per cent. A test occlusion was performed to test for colonic

[5] Oxygen level are expressed as a percentage of oxygenated haemoglobin compared to total haemoglobin (oxygenated + deoxygenated haemoglobin)

ischaemia, which if evident would require the patient to undergo open surgery rather than EVAR. The CMOS did not drop to levels that would indicate colonic ischaemia and the abdominal aortic aneurysm (AAA) was successfully treated. The patient was monitored for two days and showed no signs of colonic ischaemia (Lee et al 2008) (level IV diagnostic evidence).

Another study investigating open or EVAR repair of AAA used the T-Stat system to monitor CMOS during surgery. There were 25 subjects in the study and both CMOS and buccal oxygen levels were measured. The buccal mucosal oxygen levels were used as a comparator to verify the CMOS values were truly local values and not a reflection of systemic oxygen levels. The average recovery time to baseline after the procedures were completed was 6.4 ± 3.3 mins. Colonic ischaemia was not detected during or after the procedure. Results are shown in Table 2 (Lee et al 2006) (level IV diagnostic evidence).

Table 3 T-Stat determined oxygen levels during various procedures

T-Stat measurement	Oxygen level[6] (n=25)
Baseline CMOS	55.8 ± 8.0 %*
Test CMOS	25.7 ± 17.4 % (p < 0.001)
Post-test CMOS	56.5 ± 10.3 %*
Pre-surgical baseline CMOS	56.0 ± 9.2 %#
Surgical CMOS	14.8 ± 18.6 % (p < 0.0001)
Post-surgery CMOS	55.7 ± 5.7 %#
Buccal mucosal oxygen levels at all times	82 ± 6 %&

* Not significantly different, # Not significantly different and dropped to 64 ± 5 % in two patients with significant bleeding

The evidence on the T-Stat is preliminary in that it lacks longer term outcomes. Studies comparing populations that do and do not receive diagnosis using the T-Stat are needed to see if use of the device provides a benefit over current methods of ischaemia management. Despite this the studies show that important local information about oxygenation is provided by the T-Stat monitor and this fulfils a gap in current monitoring capabilities.

2009 COST IMPACT

Endovations Pty Ltd intends to market the T-Stat monitoring device in Australia and propose to launch the product in April 2009 at the Perinatal Society of Australia and New Zealand meeting in Darwin. The approximate Australian market price for the monitor alone is $AUD 40,000 (depending on individual negotiations and exchange rates). The price for the one-use consumables has not been finalised as yet. T-Stat training will be provided by a team of medical specialists from Endovations (personal communication: Endovations).

[6] Oxygen level are expressed as a percentage of oxygenated haemoglobin compared to total haemoglobin (oxygenated + deoxygenated haemoglobin)

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

2009 SUMMARY OF FINDINGS

The studies presented here were of low quality evidence as there is no high quality standard to use as a reference control for human studies. Nevertheless the T-Stat allowed tissue oxygen levels to be monitored during a variety of induced or real life medical procedures. Larger studies with clinical outcomes are required.

2009 HEALTHPACT ACTION:

Although there is only limited, preliminary evidence on the use of the T-Stat system, it may be useful to inform targeted resuscitation decision making. Therefore HealthPACT recommend that this technology be monitored for further information in 12-months time.

2009 NUMBER OF INCLUDED STUDIES

Total number of studies	
Level IV diagnostic evidence	3

2009 REFERENCES:

Benaron, D. A., Parachikov, I. H. et al (2004). 'Continuous, noninvasive, and localized microvascular tissue oximetry using visible light spectroscopy', *Anesthesiology*, 100 (6), 1469-1475.

Lee, E. S., Bass, A. et al (2006). 'Intraoperative colon mucosal oxygen saturation during aortic surgery', *J Surg Res*, 136 (1), 19-24.

Lee, E. S., Pevec, W. C. et al (2008). 'Use of T-Stat to predict colonic ischemia during and after endovascular aneurysm repair: a case report', *J Vasc Surg*, 47 (3), 632-634.

Welch, M., Baguneid, M. S. et al (1998). 'Histological study of colonic ischaemia after aortic surgery', *Br J Surg*, 85 (8), 1095-1098.

SEARCH CRITERIA TO BE USED:

Mucous Membrane/blood supply/metabolism
Muscles/blood supply/metabolism
Oximetry
Oxygen/ metabolism
Spectrum Analysis/methods